This is a digital copy of a book that was preserved for generations on library shelves before it was carefully scanned by Google as part of a project to make the world's books discoverable online.

It has survived long enough for the copyright to expire and the book to enter the public domain. A public domain book is one that was never subject to copyright or whose legal copyright term has expired. Whether a book is in the public domain may vary country to country. Public domain books are our gateways to the past, representing a wealth of history, culture and knowledge that's often difficult to discover.

Marks, notations and other marginalia present in the original volume will appear in this file - a reminder of this book's long journey from the publisher to a library and finally to you.

**Usage guidelines**

Google is proud to partner with libraries to digitize public domain materials and make them widely accessible. Public domain books belong to the public and we are merely their custodians. Nevertheless, this work is expensive, so in order to keep providing this resource, we have taken steps to prevent abuse by commercial parties, including placing technical restrictions on automated querying.

We also ask that you:

+ *Make non-commercial use of the files* We designed Google Book Search for use by individuals, and we request that you use these files for personal, non-commercial purposes.

+ *Refrain from automated querying* Do not send automated queries of any sort to Google's system: If you are conducting research on machine translation, optical character recognition or other areas where access to a large amount of text is helpful, please contact us. We encourage the use of public domain materials for these purposes and may be able to help.

+ *Maintain attribution* The Google "watermark" you see on each file is essential for informing people about this project and helping them find additional materials through Google Book Search. Please do not remove it.

+ *Keep it legal* Whatever your use, remember that you are responsible for ensuring that what you are doing is legal. Do not assume that just because we believe a book is in the public domain for users in the United States, that the work is also in the public domain for users in other countries. Whether a book is still in copyright varies from country to country, and we can't offer guidance on whether any specific use of any specific book is allowed. Please do not assume that a book's appearance in Google Book Search means it can be used in any manner anywhere in the world. Copyright infringement liability can be quite severe.

**About Google Book Search**

Google's mission is to organize the world's information and to make it universally accessible and useful. Google Book Search helps readers discover the world's books while helping authors and publishers reach new audiences. You can search through the full text of this book on the web at `http://books.google.com/`

341
.N7
W812

B 453709

# Para-Aminobenzonitrile and Its Derivatives.

---

## DISSERTATION

SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN THE FACULTY OF PURE SCIENCE OF COLUMBIA UNIVERSITY.

---

BY

LOUIS ELSBERG WISE, B.A.,

NEW YORK CITY

1911

---

Easton, Pa.:
Eschenbach Printing Company.
1911.

Chemica

# Para-Aminobenzonitrile and Its Derivatives.

## DISSERTATION

SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN THE FACULTY OF PURE SCIENCE OF COLUMBIA UNIVERSITY.

BY

LOUIS ELSBERG WISE, B.A.,

NEW YORK CITY

1911

Easton, Pa.:
Eschenbach Printing Company.
1911.

TO MY MOTHER AND FATHER.

# TABLE OF CONTENTS.

ACKNOWLEDGMENT........ 6
HISTORICAL INTRODUCTION........ 7
EXPERIMENTAL PART........ 10
  Preparation of Paranitrobenzonitrile........ 10
    1. From "Nitrosamine Paste"........ 10
    2. From Pure Paranitraniline........ 11
  Preparation of *p*-Aminobenzonitrile........ 12
  Hydrochloride of *p*-Aminobenzonitrile........ 14
  Picrate of *p*-Aminobenzonitrile........ 14
  Derivatives of the Fatty Acids........ 15
    1. *p*-Formaminobenzonitrile........ 15
    2. *p*-Acetaminobenzonitrile........ 16
    3. *p*-Acetaminobenzamide........ 17
  Derivatives of the Aromatic Acids........ 18
    1. *p*-Benzoylaminobenzonitrile........ 18
    2. *p*-Nitrobenzoyl *p*-Aminobenzonitrile........ 19
    3. *p*-Benzenesulphoneaminobenzonitrile........ 19
  Derivatives of Oxalic Acid........ 20
    1. Methyl *p*-Cyanoxanilate........ 20
    2. Ethyl *p*-Cyanoxanilate........ 21
    3. Di-*p*-Cyanoxanilide........ 21
    4. *p*-Cyanphenyloxamide........ 22
    5. Mono *p*-Cyanoxanilide........ 23
  Derivatives of Succinic Acid........ 23
    1. *p*-Cyansuccinanilic Acid........ 23
    2. Silver *p*-Cyansuccinanilate........ 25
    3. Methyl *p*-Cyansuccinanilate........ 25
    4. Ethyl *p*-Cyansuccinanilate........ 26
    5. *p*-Cyansuccinanil........ 27
  Derivatives of Phthalic Acid........ 27
    1. *p*-Cyanphthalanilic Acid........ 28
    2. *p*-Cyanphthalanil........ 29
    3. Action of Absolute Alcohol and Anhydrous Hydrochloric Acid........ 29
  Derivatives of Urethane and Urea........ 30
    1. *p*-Cyanphenylurethane........ 30
    2. *p*-Carbamido-phenylurethane........ 31
    3. *p*-Cyanphenylurea........ 32
    4. Mono *p*-Cyancarbanilide........ 33
    5. Di-*p*-Cyancarbanilide........ 34
    6. Attempts to Form the Monocyanthiocarbanilide........ 35

Aldehyde Reactions........................................ 36
  1. Formaldehyde Condensation........................ 36
  2. Chloral Addition and Condensation Products............ 37
  3. Action of Benzaldehyde............................ 41
Bromination of *p*-Acetaminobenzonitrile........................ 41
Nitration of *p*-Acetaminobenzonitrile........................... 42
  1. 3-Nitro-4-acetaminobenzonitrile........................ 42
  2. Saponification of the Nitrile.......................... 43
  3. 3-Nitro-4-acetaminobenzamide......................... 45
Reduction of 3-Nitro-4-acetaminobenzonitrile.................. 46
  1. 3,4-Diaminobenzonitrile............................ 46
  2. 3,4-Diacetdiaminobenzonitrile......................... 47
  3. 3-Cyan α-Methyl Benzimidazole........................ 48
  4. Action of Tin and Acetic Acid on 3-Nitro-4-acetamino benzonitrile.................................. 50
SUMMARY.................................................. 51
BIBLIOGRAPHY.............................................. 52
BIOGRAPHICAL NOTE......................................... 53

# ACKNOWLEDGMENT.

The author takes this opportunity to thank Professor Marston Taylor Bogert, under whose direction this research was undertaken, for his many valuable suggestions, his sound counsel, and his hearty encouragement throughout the course of this work.

He assures Dr. Nelson of the Department of Organic Chemistry, of his sincere appreciation for the material aid and kind advice that have been so frequently and unhesitatingly extended to him; and he wishes to thank his fellow workers in the laboratory for the friendly assistance and excellent criticisms that have been received at their hands.

L. E. W.

ORGANIC CHEMICAL LABORATORIES,
HAVEMEYER HALL, COLUMBIA UNIVERSITY.
May, 1911.

# HISTORICAL INTRODUCTION.

The literature on the nitrile and amide of *p*-aminobenzoic acid presents little more than a number of analogies between the method of preparing these compounds, and the synthesis of their *o*- and *m*-isomers. Very few of their derivatives have been described, and in the earlier work on the *p*-nitrile, there have been such wide discrepancies between the results cf different investigators, that compilers have found it impossible to definitely state the fusion point, one of the physical constants which should characterize this compound.

In 1864, Beilstein and Reichenbach,[1] while investigating the position isomerism in the aromatic series, prepared "nitrodracylamid," a substance which they reduced with ammonium sulphide. This reduction product, obtained by them in the form of large yellow crystals carrying water of crystallization, and liquefying between 178° and 179°, could be saponified with potassium hydroxide to the corresponding aminobenzoic acid, and was thus identified as *p*-aminoamide.

Four years later, in a preliminary paper, Engler,[2] first mentioned the *p*-nitro and *p*-aminobenzonitriles, and several derivatives, which were described in more detail by the same author in 1869.[3] This chemist prepared the *p*-nitrobenzonitrile by heating together equimolecular parts of anhydrous phosphoric acid and nitrobenzamide, and distilling the product, an oil which soon solidified in the neck of the retort. The nitro-nitrile was recrystallized once from alcohol.

This mode of preparation and the properties of the compound were very nearly akin to those of the "nitrobenzonitrile" (the *m*-derivative), but its boiling and melting points were both higher. The latter is given by Engler as 139° C. By heating the substance in a sealed tube with concentrated hydrochloric acid, he obtained *p*-nitrobenzoic acid.

Para-nitrobenzonitrile dissolved in ten times its weight of a concentrated solution of ammonium sulphide with evolution of heat. On cooling, a crystalline mass was deposited, which after several recrystallizations gave yellow, star-shaped clusters of the para-aminobenzthiamide, or keeping the author's nomenclature, the "hydrosulphide of para-amidobenzonitrile."

Engler furthermore reduced para-nitrobenzonitrile to the para-amidobenzonitrile. He dissolved the nitro compound in absolute alcohol, and added zinc and concentrated hydrochloric acid. The reaction was vigorous and if carried too far yielded the benzylamine. In his description, he states that he left the substance in contact with the reducing agents for eighteen hours. At the end of this time he made alkaline with caustic soda and concentrated the solution. After most of the alcohol had evaporated, a light oil separated, which solidified on cooling. This solid deposit was washed with water, and recrystallized from alcohol. It melted at 74° C. On analysis it was identified as para-aminobenzonitrile, which was readily soluble in alcohol and ether, and difficultly soluble in hot water. It formed long, colorless needles, which were soft to the touch, and which sublimed above their melting point. The same investigator also prepared and described the hydrochloride and chlorplatinate of the para-aminobenzonitrile.

In 1874, Fricke,[4] in a research which in no way refers to the work of Engler, prepared para-nitrobenzamide from the nitrobenzoylchloride and ammonia, and by distillation with phosphorus pentoxide, obtained the same nitro-nitrile in the form of colorless leaflets, which he found difficultly soluble in cold water and alcohol, readily soluble in hot alcohol, chloroform, and acetic acid, and the melting point of which he records as 147° C. From this he readily obtained para-amidobenzonitrile[5] by means of tin and glacial acetic acid. This amino derivative crystallized in small colorless needles, which liquefied at 110° C. and whose other properties agreed with those already mentioned. He also described the hydrochloride, as well as the salts of nitric and sulphuric acid.

In 1875, Griess,[6] prepared a base by treating para-uraminobenzoic acid with phosphoric anhydride. During the reaction carbon dioxide was evolved, and water eliminated.

The product, obtained in the form of colorless, glistening prisms melted at 86° C. This was also para-aminobenzonitrile.

Reid[7] in 1899, in an extensive paper on the hydrolysis of acid amides, carefully corrected the melting point of para-aminobenzamide, which fuses at 182.9° C. (cor.); but it was not until 1903, that an article referring to the melting points of para-aminobenzonitrile appeared in the chemical literature.

In that year, Bogert and Kohnstamm,[8] after carefully repeating the work of Engler, Fricke, and Griess, using their respective methods for the preparation of para-aminobenzonitrile, and a fourth method analogous to the one outlined by Bogert and Hand,[9] obtained the nitrile in every case in the form of colorless needles, melting constantly at 85.5–86° C. (cor.), and thus corroborated the results of Griess. At the same time they described the acetamino- and propionaminobenzonitriles, as well as the para-aminobenzamide and the thiamide.

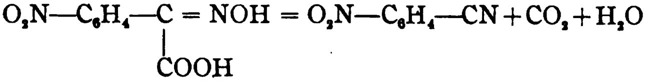
Their work has been continued and extended in this investigation, and will be described in the pages that are to follow.

Para-aminobenzonitrile was most conveniently prepared by reducing the nitro-nitrile. The latter was synthesized by a method very similar to the one described by Sandmeyer[10] in 1885. This investigator diazotized a dilute hydrochloric acid solution of para-nitraniline (kept at 25° C.) with nitrite, and added the diazo mixture to a hot aqueous solution of potassium cupro-cyanide, thus replacing the amino by the nitrile radical. His product was very difficult to purify, and could be completely separated from the side products only by sublimation. The para-nitrobenzonitrile thus obtained, formed light-yellow, feathery crystals, melting at 146° C.

In 1895, Hantzsch and Schulze,[11] in their studies on the cyanides of the syn- and the anti-nitro-diazo benzols, prepared the same compound by treating the labile $O_2N—C_6H_4—N=N—CN$ with powdered metallic copper. They gave the melting point as 147° C.

In the same year, Claus,[12] in a note referring to the previous work of Langen,[13] says that no para or ortho nitro benzonitriles were isolated in the direct nitration of benzonitrile.

Recently (1909), Borsche,[14] investigating the reactivity of the methylene group, in para and orthophenylacetic acid ethyl ester, incidentally obtained paranitrobenzonitrile, by heating paranitrophenylglyoxylic acid oxime. The reaction may be represented as follows:



$$\mathrm{O_2N{-}C_6H_4{-}}\underset{\displaystyle \mathrm{COOH}}{\underset{|}{\mathrm{C}}}\mathrm{=NOH = O_2N{-}C_6H_4{-}CN + CO_2 + H_2O}$$

The melting point of this product, which crystallizes in pale yellow leaflets, lies at 149° C.

## EXPERIMENTAL PART.*

### PREPARATION OF PARANITROBENZONITRILE.

### 1. *From "Nitrosamine" Paste.*

The starting product used in this synthesis was procured through the courtesy of the "Badische" Company.[15] It is a heavy brown paste which contains approximately 25 per cent. of the sodium salt of para-nitrophenylnitrosamine, mixed with an amount of nitrite[16] necessary to convert it to the diazonium compound. The diazotization was carried out as follows:

Two hundred and twenty-five grams of the paste were mixed with 720 cubic centimeters of cold water, the temperature kept below 18° C. and 75 grams of hydrochloric acid (about 30 per cent.) gradually added, with gentle stirring. The resulting solution, containing a dark suspended precipitate, was set aside in a refrigerator for about an hour. It was then filtered or siphoned off, and slowly added to a

*EXPLANATORY NOTE.—The melting points recorded in this dissertation (unless otherwise stated) were taken in sealed melting-point tubes, using a sulphuric acid bath as heating medium. Slight sintering or softening just below the point of fusion has not been thought worthy of special mention.

All nitrogen determinations have been made according to the method of Dumas; bromine has been determined by the Carius method.

solution of 65 grams of crystallized copper sulphate in about 410 cubic centimeters of water, to which had been added 75 grams of potassium cyanide. The temperature of the cyanide solution was maintained at about 90° C., and after each addition of the diazo-solution, the mixture was vigorously stirred. Finally when all had been added, it was boiled for a few minutes and then allowed to cool. The brown precipitate which separated was found very difficult to purify and yielded a highly colored orange or yellow-brown product when extracted with carbon tetrachloride. Impurities persisted when other solvents such as water, chloroform, and glacial acetic acid were used. Purification by sublimation was also tried and abandoned. The yield of crude para-nitrobenzonitrile (free from copper salts) varied from about 31–43 per cent. of the theory.

### 2. *From Pure Paranitraniline.*

The method followed was analogous to the one employed by Bogert and Hand,[9] and Bogert and Beans,[17] in their preparation of the ortho- and meta-isomers, and is simply a slight modification of the "Sandmeyer reaction."[10]

In general it was found advisable to start with one-half mole of pure para-nitraniline, although the molecular weight in grams may be used without serious mechanical difficulties. Sixty-seven grams of powdered para-nitraniline were added to 100 cubic centimeters of concentrated hydrochloric acid, and after adding a small amount of water, heated until complete solution was effected. The hydrochloride was then poured into a liter and a half of water and mechanically stirred until it had cooled to 18° C. or slightly below. To this mixture, a solution of 35 grams of sodium nitrite in about 200 cubic centimeters of water was added, drop by drop, with constant stirring. The diazotization usually required from two to three hours.

From this point, the synthesis is practically identical with the one recorded above. The potassium cuprous cyanide solution was prepared by dissolving 125 grams of $CuSO_4.5H_2O$ in about a liter of water and adding thereto

140 grams of powdered potassium cyanide. The temperature of the cyanide solution was kept at about 90° C. and the mixture thoroughly agitated after each addition of the diazo compound. The time consumed during the reaction varied from one-half to three-quarters of an hour, as it was found essential to allow the nitrile formation to proceed rather slowly.

After boiling the solution for several minutes and allowing it to cool, the precipitate was filtered by suction, and the golden-brown product transferred to a large, round-bottom flask, or a well annealed wide-necked 2–3 liter glass retort, and distilled with steam. The distillate was collected in a receiver packed in ice. The distillation, although somewhat tedious, always yielded a product that needed no further purification (melting point 148° C. cor.). The best yield was 50 per cent. of the theory.

The residue in the distilling flask was highly colored, and none of its components were investigated. As suggested by Bogert and Kohnstamm,[8] it may contain diphenyl[18] or diazo-amino derivatives,[19] which would sensibly diminish the yield.

Pure para-nitrobenzonitrile crystallizes in faintly colored, greenish-yellow leaflets, melts at 147.5–148.5° C. (cor.), and possesses an odor which suggests both nitrobenzol, and benzonitrile. It is soluble in water, alcohol, acetic acid, chloroform, and carbon tetrachloride at their boiling points; sublimes readily, and is volatile with steam.

### PREPARATION OF PARA-AMINOBENZONITRILE.

The reduction of the nitro benzonitrile was readily accomplished by the use of stannous chloride in acid solution.

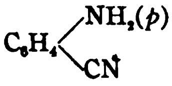
Fifty grams of pulverized para-nitrobenzonitrile were added very gradually to a solution of 250 grams of pure $SnCl_2$ in 750 cubic centimeters of concentrated hydrochloric acid. The best temperature for the reaction was found to be in the neighborhood of 45° C. Far below this point the reduction is slow, and at higher temperatures there is some danger of hydrolyzing the cyanogen radical. By initially heating the tin solution to within a few degrees of the desired point, and by carefully regulating the addition of the nitrile, this temperature may be maintained without difficulty.

During the course of the reduction, fine satiny needles of the double tin salt separated—which at the end of the reaction (after about two and one-half hours), took the form of a highly crystalline cream-like paste. This was kept over night in an ice box and filtered by suction the following morning, keeping the temperature at about 10° C. during the filtration. The salt was then dissolved in roughly $1^1/_2$ liters of water, the solution filtered to remove traces of residual matter, and transferred to several large separatory funnels. Each portion was covered with a layer of ether, and cooled with cracked ice. The free base was liberated by the slow and cautious addition of a strong solution of caustic soda.

A heavy precipitate, carrying with it compounds of tin, was thrown out of solution but redissolved in an excess of the alkaline liquor, while the amine was almost instantaneously taken up by the ethereal layer. Three extractions with ether were found sufficient. The non-aqueous layers were combined, dried with calcium chloride, and the ether carefully evaporated.

The brown crystalline product thus obtained was sometimes used directly, more often crystallized once from hot water.* The dry substance prepared by this method without further purification melted at about 86° C. (uncor.). The yields ordinarily varied between 70 and 75 per cent. of the theory.

The physical properties of para-aminobenzonitrile as described by Bogert and Kohnstamm,[8] may be summarized



$$C_6H_4\begin{cases}NH_2(p)\\CN\end{cases}$$

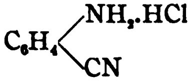
---

*Note.—When the product is crystallized from water, the mother liquors on concentrating, yield appreciable amounts of impure *p*-aminobenzonitrile. The necessity of evaporating to low bulk is obviated by simply adding a few cubic centimeters of acetic anhydride to the warm solution and heating for a few minutes on the hot plate. On cooling, a voluminous crystalline precipitate of nearly pure *p*-acetaminobenzonitrile is obtained. This derivative is one of the best tests for the presence of *p*-aminobenzonitrile, and will be described in detail.

as follows: The pure compound melts at 85.586° -C. (cor.), and crystallizes in long, colorless prisms or in compact plates. A mixture of chloroform and petroleum ether yields large crystals on careful evaporation. It is very soluble in the common alcohols, ether, ethyl acetate, benzol, chloroform, acetone, glacial acetic acid; difficultly soluble in carbon bisulphide and carbon tetrachloride, and in cold water, although fairly soluble in this solvent at its boiling point, and nearly insoluble in the petroleum solvents. In the course of this work, its ready solubility in other liquids such as pyridine, benzaldehyde, etc., has been recorded.

On rubbing this substance to an impalpable powder or on heating its aqueous solution, a faint, but characteristic, pleasant odor is developed. The compound is apparently non-volatile with steam.

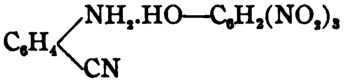
### *The Hydrochloride of Para-aminobenzonitrile.*



$$C_6H_4{<}\begin{matrix}NH_2.HCl\\CN\end{matrix}$$

This salt has already been described by Engler,[3] Fricke,[4] and by Bogert and Kohnstamm.[8] It is very conveniently prepared by dissolving the nitrile in dry ether and saturating the solution with anhydrous hydrochloric acid gas. The precipitated salt should be filtered by suction, washed with ether, and dried *in vacuo*. Under these conditions the compound takes the form of fine, colorless, micro-crystals, which are readily soluble in warm water. The yield is practically quantitative.

### *The Picrate of Para-aminobenzonitrile.*



$$C_6H_4{<}\begin{matrix}NH_2.HO{-}C_6H_2(NO_2)_3\\CN\end{matrix}$$

To prepare this derivative, 1 gram of powdered para-aminobenzonitrile was added to a benzol solution of 1.8 grams of picric acid. The mixture was heated for a few minutes, filtered, and evaporated to low bulk. On cooling, small, yellow, granular, arborescent crystals were deposited.

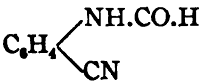
Recrystallized twice from dilute alcohol, the picrate was obtained in long, lustrous, yellow needles, melting at 150.5° C. (cor.), with decided softening about 4° below the point of fusion. The substance is readily soluble in hot alcohol, nitrobenzol, and cold acetone. It is soluble in boiling water, chloroform, and benzol, and is very difficultly soluble in ether and carbon tetrachloride. On analysis:

0.12165 gram of substance gave 21.4 cc. of moist nitrogen at 19.5° C. and 768 mm.

| | Found. | Calculated for $C_{13}H_9O_7N_5$. |
|---|---|---|
| N | 20.39 | 20.18 |

## Derivatives of the Fatty Acids.

### 1. *Para-Formaminobenzonitrile.*



$$C_6H_4\begin{cases}NH.CO.H\\CN\end{cases}$$

Two grams of the nitrile were heated for a few minutes with about 2 cubic centimeters of glacial formic acid. Complete solution ensued, and on cooling, the condensation product solidified to a dark-colored cake. This was washed with water, and repeatedly crystallized from this solvent. Some impurities persisted, so the compound was washed with ether, dissolved in hot water, thoroughly boneblacked for several hours and filtered. Colorless micro-crystals, which melted at 188–189° C. (cor.) crystallized from the filtrate. A dilute ammoniacal solution of silver nitrate, when mixed with a warm aqueous solution of the formyl-derivative, does not immediately yield a precipitate. After standing for several days in a cool place, a purplish crystalline product was obtained, which contained silver and was probably the formanilide.

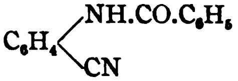
Formaminobenzonitrile is soluble in boiling alcohol, benzol, chloroform, and in cold acetone. It is dissolved by hot water, and deposited on cooling. It is insoluble in ether at its boiling point.

On analysis: 0.1141 gram of substance gave 16.2 cc. of moist nitrogen at 23° C. and 757.5 mm.

| | Found. | Calculated for $C_9H_{10}O_2N_2$. |
|---|---|---|
| N | 15.95 | 15.73 |

## Derivatives of the Aromatic Acids.

### 1. *Para-Benzoylaminobenzonitrile.*



$$C_6H_4\begin{cases}NH.CO.C_6H_5\\CN\end{cases}$$

This compound was very easily obtained by the following method:

One and one-half grams of the aminonitrile were dissolved in alcohol and about 3 cubic centimeters of benzoyl chloride poured into the solution. On stirring, a reaction took place, with the separation of a white solid. Soda was then introduced until the solution was alkaline, the mixture warmed for a short time, and then allowed to cool. More water was added, and the product filtered. Boneblacked and purified by several recrystallizations from dilute alcohol, the nitrile melted at 170–170.5° C. (cor.). It crystallizes from alcohol in pearly leaflets, from carbon tetrachloride in small plates, and from benzol in micro-crystals.

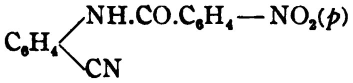
It is very soluble in cold acetone, hot ethyl and iso-amyl alcohols; soluble in cold chloroform, amyl and ethyl acetates, and in hot benzol; difficultly soluble in hot water, and carbon tetrachloride, and but slightly soluble in boiling ether. On analysis:

I. 0.1305 gram of substance gave 15.1 cc. of moist nitrogen at 22.5° C. and 752 mm.

II. 0.1325 gram of substance gave 14.9 cc. of moist nitrogen at 21° C. and 759 mm.

| | Found. | | Calculated for |
|---|---|---|---|
| | I. | II. | $C_{14}H_{10}ON_2$. |
| N | 12.94 | 12.78 | 12.62 |

### 2. *Para-Nitrobenzoyl Para-Aminobenzonitrile.*



$$C_6H_4\begin{cases}NH.CO.C_6H_4-NO_2(p)\\ CN\end{cases}$$

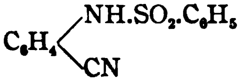
One gram of para-aminobenzonitrile was dissolved in about 50 cc. of pyridine and 1.7 grams of pure nitrobenzoylchloride added. A spontaneous reaction, which occurred with the separation of pyridine hydrochloride was completed by keeping the solution at its boiling point for a few minutes and then allowing it to cool. When poured into a large volume of cold water, the pyridine and its hydrochloride entered solution and the nitrobenzoyl derivative was precipitated. After filtering, washing with water and soda solution, and crystallizing slowly from 95 per cent. alcohol, long, pale-yellow prisms were obtained, which melted at 258–259° C. (uncor.). If the alcoholic solutions were permitted to crystallize rapidly, micro-needles were precipitated.

The substance dissolves readily in hot glacial acetic acid and nitrobenzol. It is soluble in cold acetone, rather difficultly soluble in boiling alcohol, and but slightly soluble in hot water. It is practically insoluble in ether, chloroform, and benzol at their boiling points. On analysis:

0.157 gram of substance gave 22.2 cc. of nitrogen at 24° C. and 759 mm.

| | Found. | Calculated for $C_{14}H_9O_3N_3$. |
|---|---|---|
| N | 15.83 | 15.74 |

### 3. *Para-Benzenesulphoneaminobenzonitrile.*



$$C_6H_4\begin{cases}NH.SO_2.C_6H_5\\ CN\end{cases}$$

This compound may be prepared satisfactorily from benzenesulphone chloride, in much the same way that the benzoyl derivative was obtained. It was also easily synthesized by heating para-aminobenzonitrile directly with a slight excess of the sulphone chloride. The reaction product, a pasty mass, was crystallized from dilute alcohol, washed with ether, and recrystallized from alcohol. Small, colorless, arborescent crystals melting at 175–176° C. (cor.) were obtained. They were found to be readily soluble in boiling chloroform and cold acetone; soluble in hot alcohol and benzol; difficultly soluble in hot water and partially soluble in boiling ether. On analysis:

0.1176 gram of substance gave 11.4 cc. of moist nitrogen at 22.4° C. and 756 mm.

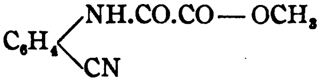
0.20685 gram of substance yielded 0.1919 gram of barium sulphate.

| | Found. | Calculated for $C_{12}H_{10}O_2N_2S$. |
|---|---|---|
| N | 10.90 | 10.85 |
| S | 12.74 | 12.42 |

## DERIVATIVES OF OXALIC ACID.

The reactions between the esters of oxalic acid and the ortho- and meta-aminobenzonitriles with the elimination of R—OH, have been studied by Reitsert and Grube,[21] and by Bogert and Beans,[22] and work on the para-compounds was begun some years ago in this laboratory[23] without reaching a definite conclusion. It seemed of some interest therefore, to continue this investigation, and if possible to prepare the derivatives of para-aminobenzonitrile which involve these condensations.

### 1. *Methyl Para-Cyanoxanilate.*



$$C_6H_4\begin{cases}NH.CO.CO-OCH_3\\CN\end{cases}$$

This ester was obtained in the following manner:

Four grams of methyl oxalate and 1.5 grams of para-aminobenzonitrile, both finely ground and intimately mixed, were heated under reflux, in an oil bath at about 110° C. for three and one-half hours. The mass melted and later resolidified, forming a pearly, pink, crystalline product. This was extracted with methyl alcohol and crystallized from this solvent in beautiful, nacreous leaflets, which kept their faint pink tint even after boneblacking and repeated crystallization. They fuse at 208.5–209.5° C. (uncor.), and are soluble in hot methyl and ethyl alcohol and boiling benzol, fairly soluble in hot chloroform, difficultly soluble in hot water, and apparently insoluble in ether. The yield is very satisfactory. On analysis:

0.1437 gram of substance gave 0.3089 gram of carbon dioxide and 0.0549 gram of water.

0.1387 gram of substance gave 17 cc. of moist nitrogen at 21° C. and 762 mm.

| | Found. | Calculated for $C_{10}H_8O_3N_2$. |
|---|---|---|
| C | 58.63 | 58.80 |
| H | 4.28 | 3.95 |
| N | 14.00 | 13.73 |

### 2. *Ethyl Para-Cyanoxanilate.*

$$C_6H_4\begin{cases}NH.CO.CO—OC_2H_5\\CN\end{cases}$$

The ethyl ester was formed in an analogous way by heating 4 grams of ethyl oxalate with 1.5 grams of para-aminobenzonitrile for about three hours at 130° C. On cooling the melt by means of ice, the product separated and was repeatedly crystallized from alcohol. It is deposited from its hot alcoholic solution in small, nearly colorless prisms, possessing a flesh tint, and melting at 188.5–189° C. (cor.). It may also be crystallized from acetic acid, and is soluble in hot alcohol, chloroform, and warm acetone. It is difficultly soluble in water and practically insoluble in ether. On analysis:

0.1179 gram of substance gave 13.8 cc. of moist nitrogen at 21° C. and 749 mm.

| | Found. | Calculated for $C_{11}H_{10}O_3N_2$. |
|---|---|---|
| N | 13.13 | 12.85 |

### 3. *Di-para-Cyanoxanilide.*

$NC—C_6H_4—NH.CO.CO—NH—C_6H_4—CN.$

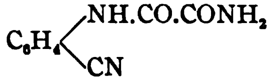
A mixture of equal parts of para-aminobenzonitrile and ethyl oxalate was heated for five and one-half hours in an oil bath at 160–210° C. The result was a brown crystalline mass which consisted of oxanilide mixed with an appreciable amount of para-cyanoxanilic acid ester. The latter was removed by repeatedly extracting the melt with boiling alcohol, in which the oxanilide is insoluble. The residual crystalline product was nearly colorless, and practically pure. It may be further purified by crystallizing from aniline. It does not fuse below 288° C. (uncor.), which was the temperature limit reached in the sulphuric acid bath.

The compound is apparently insoluble in glacial acetic acid, benzol, ether, ethyl and amyl alcohol, and nitrobenzol at their boiling points.* It is rather difficultly soluble in hot aniline and very difficultly soluble in boiling phenol. On analysis:

0.10105 gram of substance (without recrystallization) gave 17.3 cc. of moist nitrogen at 24.5° C. and 766.5 mm.

|  | Found. | Calculated for $C_{16}H_{10}O_2N_4$. |
|---|---|---|
| N | 19.33 | 19.32 |

4. *Para-Cyanphenyloxamide.*



$$C_6H_4\left\langle\begin{array}{l}NH.CO.CONH_2\\CN\end{array}\right.$$

A small amount of ethyl cyanoxanilate was added to a concentrated ammonium hydroxide solution and digested on the hot plate for about one-half hour. The mixture was then diluted with water and allowed to stand over night. The product was filtered, recrystallized from glacial acetic acid and washed with ether. It formed minute, nearly colorless crystals, which melted well above 300° C. The derivative is soluble in hot nitrobenzol and glacial acetic acid, very slightly soluble in boiling alcohol, and apparently insoluble in water, ether, chloroform, benzol, and amyl-acetate.

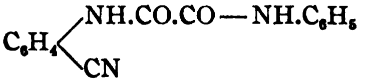
---

* A number of these solubilities have been taken directly from the thesis of Mr. Williamson, who obtained this compound but did not identify it by analysis.

On analysis: 0.12845 gram of substance gave 25.5 cc. of moist nitrogen at 20° C. and 747 mm.

| | Found. | Calculated for $C_9H_7O_2N_3$. |
|---|---|---|
| N | 22.32 | 22.23 |

### 5. *Mono Para-Cyanoxanilide.*



$$C_6H_4\begin{cases}NH.CO.CO-NH.C_6H_5\\CN\end{cases}$$

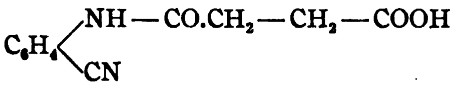
Somewhat less than a gram of ethyl para-cyanoxanilate was heated with an excess of aniline, in the presence of anhydrous zinc chloride. A transparent solution was formed, and was kept at its boiling point for about fifteen minutes. On cooling, the mixture solidified, and was dissolved in a large volume of hot alcohol, from which a crystalline, slightly colored product was deposited. This was freed from zinc salts by recrystallizing twice from dilute acetic acid. The purification was accomplished by dissolving the substance in glacial acetic acid, filtering, and diluting the filtrate with water. In this way, long, silky, prismatic needles were obtained, which on further crystallization from alcohol gave a pure product melting at 246° C. (uncor.). Deposited from alcohol, the oxanilide takes the form of minute, colorless crystals, soluble in hot glacial acetic acid and cold chloroform, and apparently insoluble in water and ether. On analysis:

0.1046 gram of substance gave 14.6 cc. of moist nitrogen at 18.5° C. and 753 mm.

| | Found. | Calculated for $C_{15}H_{11}O_2N_3$. |
|---|---|---|
| N | 15.93 | 15.85 |

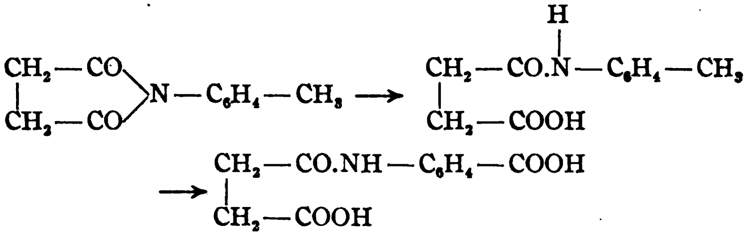
## DERIVATIVES OF SUCCINIC ACID.

### 1. *Para-Cyansuccinanilic Acid.*



$$C_6H_4\begin{cases}NH-CO.CH_2-CH_2-COOH\\CN\end{cases}$$

Michael[24] first prepared the so-called "oxy-succinyl paraamidobenzoic acid" by hydrolyzing the para-methylsuccinanil, and oxidizing the methyl to the carboxyl group.



The derivative described below is the nitrile of this acid, and was readily prepared by the following method:

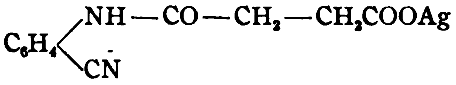
Four grams of para-aminobenzonitrile were dissolved in a small amount of chloroform, and added to a chloroformic solution of 3.5 grams of freshly distilled succinic anhydride. The clear solution, after boiling under reflux for about half an hour, became slightly turbid. This turbidity was soon followed by a deposition of fluffy crystals. After cooling and filtering, the mother liquor, when boiled under a return condenser for several hours longer, yielded another crop of the same product. Still more was obtained from the filtrate by repeating this operation. The total yield (after washing the substance thoroughly with ether and chloroform) amounted to about 4.6 grams. On repeating the experiment with about 6 grams of the nitrile and 5.2 grams of the anhydride, a yield of 8.36 grams was obtained.

The reaction is apparently a rather slow one, and seems to be aided by the presence of small amounts of moisture. The acid precipitated from chloroform is nearly pure. It melts at 213° C. (uncor.). Recrystallized from water, it separated in the form of colorless prismatic rods, melting at 213–214° C. (uncor.). Para-cyansuccinanilic acid is soluble in acetone, hot alcohol, boiling water and in glacial acetic acid. It is insoluble in ether, chloroform, and benzol. It dissolves readily in solutions of ammonia, and the carbonates, and gives a deep reddish-brown solution with ferric chloride, which, after heating for a short while, and cooling, precipitates the brown iron salt.

On analysis: 0.1419 gram of substance gave 16 cc. of moist nitrogen at 20.5° C. and 764 mm.

| | Found. | Calculated for $C_{11}H_{10}O_3N_2$. |
|---|---|---|
| N | 12.94 | 12.85 |

### 2. *Silver Para-Cyansuccinanilate.*



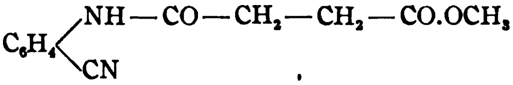
$$C_6H_4\begin{cases}NH-CO-CH_2-CH_2COOAg\\CN\end{cases}$$

This salt was prepared by dissolving the acid in a solution of ammonia, warming the mixture, and then adding an excess of silver nitrate. After heating to expel most of the free ammonia, the silver derivative was deposited, taking the form of slightly colored crystals. The clear mother liquor on cooling yielded another crystallization, which was somewhat purer than the first. The substance crystallizes in needles, that are colorless or faintly purple. It is very soluble in ammonia, partially soluble in hot, and insoluble in cold water. On analysis:

0.1463 gram of substance gave 0.0488 gram of metallic silver.

| | Found. | Calculated for $C_{11}H_9O_3N_2Ag$. |
|---|---|---|
| Ag | 33.36 | 33.20 |

### 3. *Methyl Para-Cyansuccinanilate.*



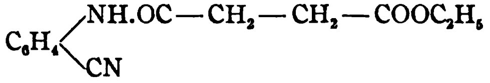
$$C_6H_4\begin{cases}NH-CO-CH_2-CH_2-CO.OCH_3\\CN\end{cases}$$

One gram of the cyansuccinanilic acid was suspended in absolute methyl alcohol and a rapid stream of dry hydrochloric acid gas passed into the mixture until a clear solution resulted. After continuing this treatment for a few minutes longer, the product was thrown out of the liquid by pouring the alcoholic solution into cold water, or preferably on cracked ice. The white, finely divided, crystalline precipitate was filtered, washed with water, and shaken with a solution of sodium carbonate to dissolve any unchanged acid. It crystallized from dilute methyl alcohol in delicate, lustrous, silver-white scales which melted 155–156° C. (cor.). The ester is easily soluble in cold chloroform and acetone, and soluble in hot methyl alcohol, boiling water, and in ether at its boiling point. It is apparently insoluble in the lower petroleum fractions. On analysis:

0.1224 gram of substance gave 12.8 cc. of moist nitrogen at 18° C. and 769.5 mm.

| | Found. | Calculated for $C_{12}H_{12}O_3N_2$. |
|---|---|---|
| N | 12.24 | 12.07 |

### 4. *Ethyl Para-Cyansuccinanilate.*



$$C_6H_4\begin{cases}NH.OC-CH_2-CH_2-COOC_2H_5\\CN\end{cases}$$

The preparation of this compound was entirely analogous to that of the methyl ester. Absolute alcohol was used and care taken to preserve anhydrous conditions throughout the course of the esterification. It was noticed that when the mixture, after passage of the hydrochloric acid gas, was poured on ice, no precipitate was formed. Furthermore miscible and immiscible solvents failed to precipitate the ester, and it was only on shaking out repeatedly with ether and evaporating these ethereal solutions, that the product was finally obtained.

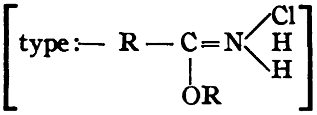
On repeating the experiment, with a much smaller quantity of absolute alcohol, the product separated very satisfactorily, when the solution was poured on cracked ice. Precipitated by this method, it should be thoroughly shaken with a potassium carbonate solution to insure removal of the remaining acid.

When heated with water, the ester first melts to an oil, but on addition of a very small amount of alcohol, it readily enters solution, and is deposited on cooling, in nacreous, silvery leaflets. It melts sharply at 111° C. (cor.), and is readily soluble in chloroform and acetone, soluble in ethyl alcohol, ether, hot benzol, and insoluble in petroleum ether.

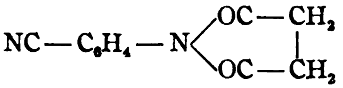
On analysis: 0.08585 gram of substance gave 8.65 cc. of moist nitrogen at 23° C. and 772 mm.

| | Found. | Calculated for $C_{13}H_{14}O_3N_2$. |
|---|---|---|
| N | 11.54 | 11.38 |

In neither of the ester formations recorded above were there any evidences of the production of hydrochlorides of the corresponding benzimino esters,[25]



### 5. *Para-Cyansuccinanil.*



By eliminating one molecule of water from the para-cyansuccinanilic acid, the anil may be readily obtained. The acid was added to an excess of acetic anhydride and the solution evaporated to a heavy, dark-brown oil. This was mixed with a large amount of water and boiled to destroy the remaining anhydride. The solution thus formed was filtered and allowed to crystallize. On cooling, large crystals were deposited, which on recrystallization from water, separated in the form of large, opaque, ivory-colored needles resembling splinters. The substance is soluble in cold acetone and chloroform, boiling alcohol, hot water, benzol, glacial acetic acid, amyl acetate, and iso-amyl alcohol. It is apparently insoluble in boiling ether. It melts at 170° C. (cor.). On analysis:

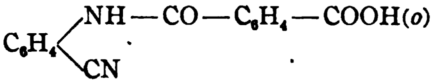
0.1245 gram of substance gave 15.65 cc. of moist nitrogen at 23° C. and 754 mm.

| | Found. | Calculated for $C_{11}H_8O_2N_2$. |
|---|---|---|
| N | 14.05 | 14.00 |

## DERIVATIVES OF PHTHALIC ACID.

The usual striking analogies existing between derivatives of phthalic and succinic acids led to the preparation of the para-cyanphthalanilic acid. This is in fact the nitrile of the acid which was prepared by Michael,[24] in a manner quite analogous to the one already described for the production of his substituted succinic acid.

### 1. *Para-Cyanphthalanilic Acid.*



$$C_6H_4\left\langle\begin{array}{l}NH-CO-C_6H_4-COOH(o)\\ CN\end{array}\right.$$

Three and one-tenth grams of phthalic anhydride, recently sublimed, were dissolved in about 50 cc. of chloroform, and a solution of 2.5 grams of para-aminobenzonitrile in 25–30 cc. of chloroform added. The mixture was heated in a flask and kept at the boiling point of the solvent for a few minutes. It then became cloudy, and on rotating the vessel deposited a paste of faintly colored, silky needles. The mother liquor, when heated on a water bath, yielded a second, and finally a third crop of crystals. The total yield of pure substance approximated 5 grams, and was therefore nearly quantitative. Recrystallized from chloroform, colorless, fine needles were obtained, whose melting point, varied with the rate of heating. When plunged into the bath at 145° C. they fused at about 163° C. (cor.). The uncertainty of this melting point shows an interesting property quite analogous to the one characterizing phthalic acid itself.

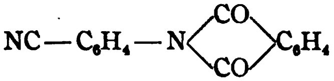
The acid is very soluble in cold alcohol, soluble in glacial acetic acid, warm acetone, hot amyl acetate and in boiling water. It is appreciably soluble in cold chloroform, somewhat soluble in boiling benzol and toluol, and very soluble in boiling ether. It may be crystallized from chloroform or dilute alcohol, being deposited from the latter in fine, hair-like needles.

Heated above its melting point, the cyanphthalanilic acid yields a sublimate of fine, colorless needles, closely resembling phthalic anhydride. On examination it was found to be the cyanphthalanil. On analysis:

0.1277 gram of the acid gave 11.8 cc. of moist nitrogen at 22° C. and 779 mm.

| | Found. | Calculated for $C_{15}H_{10}O_3N_2$. |
|---|---|---|
| N | 10.73 | 10.53 |

## 2. *Para-Cyanphthalanil.*



This compound is formed by the elimination of one molecule of water, when the acid is heated above its melting point. Obtained by this method, it forms a white sublimate melting at 187° C. (cor.). The substance is more readily prepared in the presence of a dehydrating agent.

One gram of para-cyanphthalanilic acid was gradually added to an excess of acetic anhydride and slowly evaporated to a dark-colored syrup. An evolution of heat marked the course of the reaction. On cooling, the syrup crystallized to a layer of brown rosettes. These were digested with hot water and filtered. The product crystallized from alcohol in feathery clusters of silky, colorless needles, melting at 187° C. (cor.). This substance, intimately mixed with the sublimate described above, liquefied without depression at the same point.

The phthalanil is readily soluble in cold glacial acetic acid, benzol, toluol, and nitrobenzol, in chloroform, acetone, and boiling ethyl alcohol and isoamyl alcohol. It is soluble in ether and amyl acetate and difficultly soluble in hot water. It sublimes and is apparently volatile with steam. On analysis:

0.1129 gram of substance gave 11.4 cc. of moist nitrogen at 21.5° C. and 758 mm.

| | Found. | Calculated for $C_{15}H_8O_2N_2$. |
|---|---|---|
| N | 11.44 | 11.29 |

## 3. *Action of Absolute Alcohol and Anhydrous Hydrochloric Acid.*

In an attempt to form the ethyl ester of cyanphthalanilic acid, by the method outlined above (see methyl cyansuccinanilate), a product was obtained when the alcoholic solution was poured into cold water, which crystallized from dilute alcohol in small, colorless, shimmering crystals. Their melting point was uncertain but since they appeared perfectly homogeneous, an analysis was made with the following result:

0.1185 gram of the substance gave 10.9 cc. of moist nitrogen at 22° C. and 763 mm.

| | Found. | Calculated for | |
|---|---|---|---|
| | | $C_{17}H_{14}O_3N_2$. (Ester.) | $C_{15}H_{10}O_3N_2$. (Acid.) |
| N | 10.46 | 9.53 | 10.53 |

This result apparently indicated that the parent acid had not been affected, but on closer examination, it was found that this product was insoluble in solutions of the alkali carbonates (in which the phthalanilic acid readily dissolves). After washing the substance thoroughly with a solution of potassium carbonate, another analysis gave the figures recorded below.

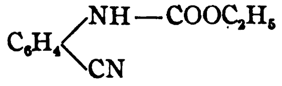
0.0995 gram of substance gave 9.4 cc. of moist nitrogen at 23.5 C. and 762° mm.

| | Found. |
|---|---|
| N | 10.65 |

Heated in an open melting point tube, the substance fused at about 140° C. (uncor.). The temperature was then carried up to about 175° C. On cooling, the melt solidified to a crystalline mass, which liquefied at approximately 180° C. (uncor.). No theory has been found that accounts for this reaction, and the work, owing to the insignificant yield, was not repeated.

## DERIVATIVES OF URETHANE AND UREA.

### 1. *Para-Cyanphenylurethane.*



$$C_6H_4\begin{cases}NH-COOC_2H_5\\CN\end{cases}$$

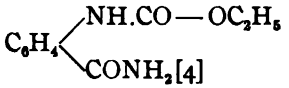
One gram of para-aminobenzonitrile was dissolved in alcohol, diluted with a little water, and a small amount of sodium carbonate added. Several cubic centimeters of ethyl chlorformate were then poured into the mixture. There was no apparent reaction in the cold, but on heating, carbon dioxide was evolved, and if an insufficient amount of water was present, an oil separated from the slightly alkaline solution. This oil remained unchanged, even at a low temperature, but on further addition of water, it was instantaneously converted to a white crystalline solid. (In the presence of larger amounts of water, the above phenomenon did not occur). The precipitate was filtered, washed with water, and recrystallized twice from dilute alcohol.

The urethane crystallizes in colorless, prismatic needles, liquefying at 116–117° C. (cor.), and in melting gives a faint but characteristic odor, suggestive of pineapple. The compound is soluble in cold acetone, benzol, methyl and ethyl alcohols, ether, and chloroform, and is partially soluble in boiling water, in which it first melts to an oil. On analysis:

0.1141 gram of substance gave 15.1 cc. of moist nitrogen at 22.5° C. and 762.5 mm.

| | Found. | Calculated for $C_{10}H_{10}O_2N_2$. |
|---|---|---|
| N | 15.00 | 14.74 |

### 2. *Para-Carbamidophenylurethane.*



$$C_6H_4\begin{cases}NH.CO-OC_2H_5\\ CONH_2[4]\end{cases}$$

Para-Cyanphenylurethane was heated for several hours on a water bath under reflux, with a 3 per cent. solution of hydrogen peroxide (rendered alkaline with sodium carbonate). The mixture was then cooled and the product filtered, washed with a small quantity of alcohol, and crystallized from dilute alcohol. The compound separated in slender, colorless needles, which were repeatedly crystallized from the same solvent. The melting point, even after this purification varied somewhat with the rate of heating. When heated rapidly, the substance fused at 232.5° C. (uncor.), and became solid again, just above this point. Resolidification above the point of fusion invariably occurred.

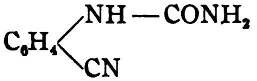
Lack of material did not permit a very thorough investigation, but a gram of the amide heated above its melting point was decomposed into ammonia, and at least two solid compounds, which could be roughly separated by the use of chloroform. One of these substances did not melt above 305° C. (uncor.), and was apparently insoluble in the common solvents. Neither of them could be identified owing to the fact that less than 0.6 gram of the crude mixture was obtained in this experiment.

The phenylurethane carbamide may be obtained in minute crystals from benzol, and in needles from dilute alcohol. It is soluble in cold glacial acetic acid, alcohol, hot benzol, and boiling water. It is difficultly soluble in boiling ether, acetone, and chloroform. On analysis:

0.1226 gram of substance gave 14.9 cc. of moist nitrogen at 22° C. and 753 mm.

| | Found. | Calculated for $C_{10}H_{12}O_3N_2$. |
|---|---|---|
| N | 13.64 | 13.46 |

### 3. *Para-Cyanphenylurea.*



$C_6H_4\langle{}^{NH-CONH_2}_{CN}$

Para-uraminobenzoic acid was made by Griess,[26] by the fusion of para-aminobenzoic acid with urea or by the action of potassium cyanate upon the hydrochloride of the same acid. This reaction is quite analogous to the one used in the formation of its nitrile.

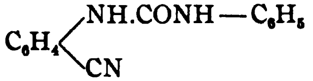
This compound was prepared by dissolving 1.4 grams of the pulverized hydrochloride of para-aminobenzonitrile (the preparation of which has already been described) in warm water, filtering, and adding to this filtrate an aqueous solution of 0.76 gram of pure potassium cyanate. An immediate precipitation resulted. The precipitate was dissolved in hot water, boneblacked, and recrystallized twice from water. The substance separated in colorless micro-needles, which melted at 207.5–208.5° C. (uncor.), and were found easily soluble in hot ethyl and iso-amyl alcohols, soluble in boiling acetone and hot water, and apparently insoluble in ether, chloroform, and benzol. On analysis:

0.1086 gram of substance gave 25.7 cc. of moist nitrogen at 25.5° C. and 757.5 mm.

| | Found. | Calculated for $C_8H_7ON_3$. |
|---|---|---|
| N | 26.24 | 26.09 |

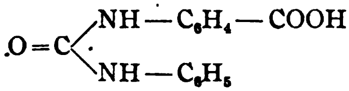
An attempt to form the urea by digesting the para-cyanphenylurethane with concentrated ammonia proved futile, and a similar experiment with a strong solution of monomethyl amine, in the hope of obtaining the para-cyanphenyl methylurea was also unsuccessful. In both cases the starting material was recovered.

### 4. *Mono Para-Cyancarbanilide.*



$$C_6H_4 < \begin{matrix} NH.CONH-C_6H_5 \\ CN \end{matrix}$$

The acid corresponding to this nitrile was prepared by Guareschi[27] by fusing para-aminobenzoic acid with phenylurea. The product, termed phenyluraminobenzoic acid, has the formula:



$$O=C < \begin{matrix} NH-C_6H_4-COOH \\ NH-C_6H_5 \end{matrix}$$

To prepare the nitrile, 1 gram of para-aminobenzonitrile was dissolved in benzol, and an excess of phenylcyanate added. Since there was no apparent reaction in the cold, the yellow solution was gently heated on a water bath and stirred. After a short while, a light-yellow, crystalline paste separated and was allowed to stand over night. It was then filtered and recrystallized to constant melting point from alcohol. The yield was very satisfactory.

The carbanilide crystallizes in colorless, silky needles, forming feathery clusters, which melt at 198.5° C. (cor.). It is readily soluble in cold acetone, glacial acetic acid, and alcohol, soluble in hot benzol and cold chloroform, appreciably soluble in boiling ether, and difficultly soluble in hot water. The dry substance, when pulverized, formed a fluffy mass, which owing to its extreme lightness could not be easily introduced into the "nitrogen tube" without loss. On analysis:

0.10505 gram of substance gave 0.27085 gram of carbon dioxide and 0.0467 gram of water.

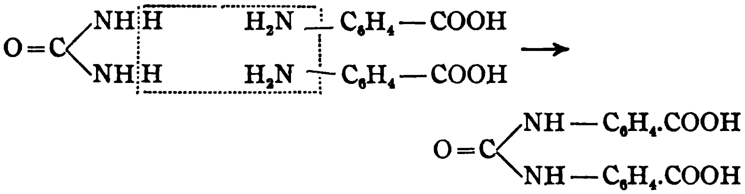
0.15825 gram of substance gave 24.3 cc. of moist nitrogen at 20.5° C. and 753.5 mm.

| | Found. | Calculated for $C_{14}H_{11}ON_3$. |
|---|---|---|
| C | 70.32 | 70.85 |
| H | 4.98 | 4.68 |
| N | 17.37 | 17.73 |

### 5. *Di-para-Cyancarbanilide.*

$NC{-}C_6H_4{-}NH{-}CO{-}NH{-}C_6H_4{-}CN$

The possibility of forming two products by fusing urea with para-aminobenzoic acid is apparent. One has already been mentioned, the other was formed by Griess,[26] by condensing two molecules of the acid with one of the urea.



$$O{=}C\begin{cases} NH\,\vdots\, H \quad H_2N\,\vdots\, C_6H_4{-}COOH \\ NH\,\vdots\, H \quad H_2N\,\vdots\, C_6H_4{-}COOH \end{cases} \longrightarrow O{=}C\begin{cases} NH{-}C_6H_4.COOH \\ NH{-}C_6H_4.COOH \end{cases}$$

This is the acid corresponding to the di-para-cyancarbanilide.

This derivative was prepared by dissolving 1 gram of para-aminobenzonitrile in benzol and adding a solution of phosgene in a mixture of benzol and toluol. An immediate precipitation took place without apparent generation of heat, and a light yellow precipitate was formed. After standing over night, this was filtered and crystallized from dilute alcohol. It formed small, white needles, which melted at 273° C. (uncor.). The compound is soluble in hot alcohol, but insoluble or difficultly soluble in boiling water, chloroform, and ether. The yield is poor. On analysis:

0.1078 gram of substance gave 19.9 cc. of moist nitrogen at 20° C. and 766 mm.

| | Found. | Calculated for $C_{15}H_{10}ON_4$. |
|---|---|---|
| N | 21.28 | 21.38 |

### 6. *Attempts to Form the Mono-cyan Thio-carbanilide.*

Efforts to condense the nitrile with phenyl mustard oil were apparently successful, but only one product, thiocarbanilide, was identified in the condensation mixtures.

Heating equal amounts of para-aminobenzonitrile with phenyl mustard oil directly, between 140–150° C. for one and one-half hours, resulted in a brown resin, from which nothing could be isolated. Heating equimolecular amounts of the two substances dissolved in toluol also led to no result. Another attempt to gain the condensation using amyl alcohol as condensing medium, yielded 2 products, which were separated by fractional crystallization. One of these, the less soluble compound, crystallized from alcohol in prismatic needles melting at 154.5° C. (uncor.), while the other, still very impure, melted below 100° C. In this experiment only 50 mg. of the higher melting substance were obtained.

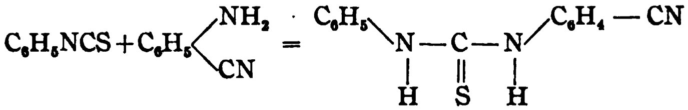
On repeating this work under apparently similar conditions, 2 grams of para-aminobenzonitrile were dissolved in about 50 cc. of isoamyl alcohol and to this a similar alcoholic solution of 2–3 grams of phenyl mustard oil was added. The mixture evaporated to low bulk and allowed to stand in the refrigerator, yielded crystals, which, when washed with ether and recrystallized from dilute ethyl alcohol, formed colorless leaflets which melted at 148–149° C. (uncor.), and which were soluble in acetone and alcohol, and insoluble in water. This was thio-carbanilide. On analysis:

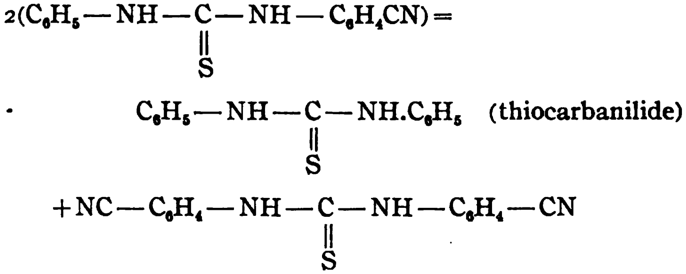
0.0828 gram of substance gave 9.1 cc. of moist nitrogen at 21.5° C. and 759.5 mm.

| | Found. | Calculated for $C_{13}H_{12}N_2S$. (Thiocarbanilide.) |
|---|---|---|
| N | 12.48 | 12.28 |

Pure thiocarbanilide melts a few degrees higher and a mixture of the two substances showed no depression of melting point.

Unfortunately, lack of time has not permitted a further investigation of the exact conditions, which led to the formation of the product melting at 154.5° C. (uncor.), and which is probably the para-cyanthiocarbanilide. A theory which perhaps explains the formation of thiocarbanilide is expressed by the following equations:

(1) 

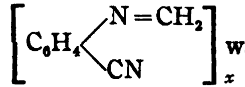
(2) 

$$2(C_6H_5-NH-\underset{\underset{S}{\|}}{C}-NH-C_6H_4CN) = C_6H_5-NH-\underset{\underset{S}{\|}}{C}-NH.C_6H_5 \text{ (thiocarbanilide)} + NC-C_6H_4-NH-\underset{\underset{S}{\|}}{C}-NH-C_6H_4-CN$$

The *di-para-cyanthiocarbanilide*, however, was never isolated, and possibly suffers further decomposition.

### Aldehyde Reactions.

#### 1. *Formaldehyde Condensation.*

Following the method outlined by Grube,[28] 1 gram of para-aminobenzonitrile was dissolved in acetone and about 3 cc. of an aqueous 40 per cent. solution of formaldehyde added. Under these conditions, Grube found that in the case of the *o*-aminobenzonitrile, a methylene derivative of the type  was formed.

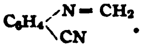
The para-aminobenzonitrile, however, did not react immediately, nor did any condensation product separate on standing. After concentrating the acetone solution, and adding water, a syrupy resin was obtained, over which was deposited a layer of fine, colorless needles.

The resin, on extraction with boiling water, dissolved, leaving little residue, and the aqueous extract yielded a further deposit of colorless needles. Recrystallized several times from water and finally dissolved in acetone and precipitated with water and dried *in vacuo*, the substance melted at about 158° C. (uncor.). Microscopic examination showed a homogeneous mass of colorless, hair-like needles. The compound is very soluble in acetone, hot alcohol, and boiling chloroform. It is soluble in hot, and very difficultly soluble in cold water.

The low melting point of the substance caused surprise, since the methylene derivative of the ortho compound melted at 211–212° C.,[28] and analogous para-compounds in this series invariably have higher points of fusion than their ortho- or meta-isomers. On analysis:

I. 0.12345 gram of substance gave 24.05 cc. of moist nitrogen at 24° C. and 772 mm.

II. 0.1497 gram of substance gave 30.3 cc. of moist nitrogen at 24.5° C. and 759 mm.

| | Found. | Calculated for  $C_6H_4\begin{cases}N=CH_2\\CN\end{cases}$. | Calculated for $NC—C_6H_4—NH—CH_2—NH—C_6H_4—CN$ |
|---|---|---|---|
| N | 22.21<br>22.60 | 21.54 | 22.58 |

Judging by the results of these analyses, the compound is not an isomer of methylene ortho-aminobenzonitrile, but may be the methylene di-(para-aminobenzonitrile)

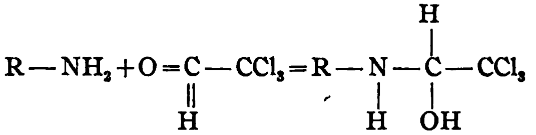
$$NC—C_6H_4—NH—CH_2—NH—C_6H_4—CN$$

or accepting the nomenclature used by Senier and Goodwin,[29] the *para-di-cyandiphenyl-methylene-diamine.*

### 2. *Chloral Addition and Condensation Products.*

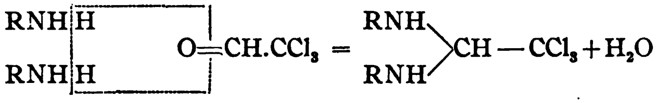
Eibner[30] described addition products obtained by treating aniline, para-toluidine, and other substituted arylamines with chloral. When the reaction proceeded slowly the addition product could be isolated and identified by analysis. When the action was violent, as in the case of the chloranilines, no intermediate addition product was obtained and the condensation product was immediately formed. The following equations indicate the trend of the reaction:

Addition:

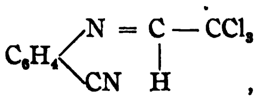


$$R-NH_2+O=\underset{\substack{\| \\ H}}{C}-CCl_3=R-\underset{\substack{| \\ H}}{N}-\overset{\substack{H \\ |}}{\underset{\substack{| \\ OH}}{C}}-CCl_3$$

Condensation:



By a method very similar to the one described in Eibner's paper, an attempt was made to prepare the addition product of para-aminobenzonitrile and chloral. Two grams of the nitrile, dissolved in ether and a small amount of gasoline, were kept in an ice bath and 2.6 grams of chloral in gasoline solution were gradually added. A precipitation of granular masses was the immediate result. This product was filtered. It was found difficultly soluble in ether, practically insoluble in chloroform and gasoline, and soluble in cold acetone, alcohol, and hot benzol. Heated with water, it decomposed, yielding para-aminobenzonitrile and chloral. It could not be obtained in pure form and the melting point was very indefinite. Chloral vapors were always evolved, when the substance was decomposed by heat. Several nitrogen analyses gave figures which indicated a Schiff's base of the formula



but the fact that this was merely coincidence was later shown by experiment. On analysis:

I. 0.1199 gram of substance (extracted with ether, and precipitated with gasoline) gave 11.6 cc. of moist nitrogen at 20° C. and 759 mm.

II. 0.1263 gram of substance (crystallized from benzol) gave 12.6 cc. of moist nitrogen at 21.5° C. and 748.5 mm.

III. 0.1471 gram of substance (dried *in vacuo*, directly after washing with ether without further purification) gave 15.2 cc. of moist nitrogen at 24.5° C. and 753 mm.

| | Found. | Calculated for $C_9H_7ON_2Cl_3$. | Calculated for $C_9H_5N_2Cl_3$. [the Schiff's base.] |
|---|---|---|---|
| N | I. 11.05 | ... | ... |
| | II. 11.16 | 10.51 | 11.31 |
| | III. 11.41 | ... | ... |

It was reasoned that if the substance were principally the Schiff's base, mixed with a small amount of the addition product, a thorough dehydration would give the former compound in pure state. The impure product (from benzol, No. II) was accordingly treated by a method similar to the one used by Diels and Seib[31] in effecting their "anhydro" condensations between the urethanes and chloral. The dry powder was added to a dilute, ice-cold solution of caustic soda, and cold acetic anhydride poured into the mixture. The resultant product crystallized from alcohol in small rosettes, which on recrystallization from the same solvent, somewhat diluted, took the form of colorless, shimmering micro-crystals fusing rather sharply at 169° C. (cor.) to a red melt. On analysis:

0.1002 gram of substance gave 13.5 cc. of moist nitrogen at 20° C. and 755 mm.

| | Found. | Calculated for the Schiff's base, $C_9H_5N_2Cl_3$. | Calculated for the dimolecular condensation product. $C_{16}H_{11}N_4Cl_3$. |
|---|---|---|---|
| N | 15.32 | 11.31 | 15.33 |

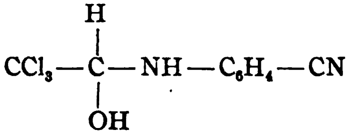
Evidentally, the mono-molecular condensation product was *not* formed. Attempts to effect the condensation between two molecules of para-aminobenzonitrile and one molecule of chloral, in order to synthesize the compound obtained by the dehydration described above, were in general, unsuccessful.

The method here used was essentially the same as the one employed by Wheeler and Weller,[32] in their work on the nitranilines, with the difference that toluol, instead of benzol, was used as solvent (cf. Bogert and Beans).[33] About 0.8 of a cubic centimeter of anhydrous chloral was added to a toluol solution of 2 grams of para-aminobenzonitrile. A precipitate immediately formed, but redissolved when the mixture was boiled under a reflux condenser for a short while. The toluol solution was then taken nearly to dryness and allowed to stand in a cool place. A brown crystalline paste was deposited, which on dissolving in hot alcohol and decolorizing with boneblack, crystallized from the diluted alcoholic filtrate in shimmering crystals melting at 167.5–168.5° C. (cor.). The substance was identical with the one described above, since a mixture of the two compounds melted at 169° C. (cor). Unfortunately the yield was very meagre and a halogen determination was accidentally lost. In trying to repeat this condensation, negative results were invariably obtained. Para-aminobenzonitrile and chloral were the end-products and no condensation product was isolated. In one of these experiments the pasty deposit from the toluol solution was examined, and found to be a mixture of para-aminobenzonitrile and what was believed to be the addition product, since on heating with water, it gave off chloral and formed the nitrile.

Owing to these difficulties and furthermore to a lack of necessary time, this interesting problem was discontinued.

To sum up the results of the chloral additions and condensations:

(*a*) Para-aminobenzonitrile probably adds chloral to form the *trichloroxyethylidene para-cyanphenamine.*



$$CCl_3-\overset{\displaystyle H}{\underset{\displaystyle OH}{C}}-NH-C_6H_4-CN$$

(*b*) The addition product, on attempted dehydration, probably passes into *trichlorethylidene di-para-cyanphenamine*,

$$CCl_3—CH=[NH—C_6H_4CN]_2,$$

a compound which was identical with one which could only be obtained once by direct condensation.

### 3. *Action of Benzaldehyde.*

Attempts to condense para-aminobenzonitrile with benzaldehyde alone to form the benzylidene derivative, invariably gave negative results. The method used was in essence the one described by Rhode,[34] in his work with para-nitraniline. One gram of para-aminobenzonitrile was added to 2 cc. of benzaldehyde and the resulting solution heated in an oil bath between 140° and 170° C., for three and one-half hours. At the end of this time the mixture, which showed no signs of solidifying, was subjected to steam distillation. Only para-aminobenzonitrile and a few milligrams of tar remained behind.

Other trials with somewhat more vigorous heating also yielded the starting products. When zinc chloride was tried as condensing agent, a heavy tar was obtained from which the substance sought could not be isolated.

## BROMINATION OF PARA-ACETAMINOBENZONITRILE.

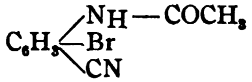
Para-acetaminobenzonitrile was dissolved in a warm solution of concentrated acetic acid and bromine added drop by drop until the solution was deep brown. After standing for some time (preferably over night), the excess of bromine was removed by boiling, and the bromination product precipitated by the addition of a large volume of water. Recrystallized several times from alcohol, the product melted at 161.5–162.5° C. (cor.). Treatment with acetic anhydride and crystallization from dilute acetic acid did not alter this melting point. The pure product gives the copper wire test for halogen. It crystallizes in long, lustrous needles, sometimes forming clusters, or in small, isolated, glassy crystals. It is freely soluble in chloroform and acetone, soluble in hot alcohol and glacial acetic acid, difficultly soluble in hot water, and slightly soluble in ether and carbon tetrachloride at their boiling points. On analysis:

0.1599 gram of substance gave 0.1277 gram of silver bromide.

0.1208 gram substance gave 12.2 cc. of moist nitrogen at 15.5° C. and 760 mm.

|  | Found. | Calculated for $C_9H_7N_2OBr$. |
|---|---|---|
| Br | 33.99 | 33.44 |
| N | 11.80 | 11.72 |

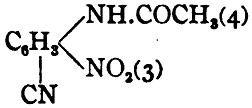
The substance is evidentally a mono-bromacetaminobenzonitrile and has the formula:



$$C_6H_3\left<\begin{matrix}NH-COCH_3\\Br\\CN\end{matrix}\right.$$

### NITRATION OF PARA-ACETAMINOBENZONITRILE.

### 1. *3-Nitro-4-Acetaminobenzonitrile.*



$$\underset{\displaystyle CN}{\underset{|}{C_6H_3}}\left<\begin{matrix}NH.COCH_3(4)\\NO_2(3)\end{matrix}\right.$$

The acid of which this is the nitrile was obtained by Kaiser,[35] through the action of cold nitric acid on para-acetaminobenzoic acid. He showed the position of the nitro group by converting the acid to ortho-phenylene diamine.

The nitrile was readily obtained by the following method: Ten grams of dry, pulverized acetaminobenzonitrile were gradually stirred into a syrup prepared by adding powdered potassium nitrate to cold, concentrated sulphuric acid. The nitration mixture was kept at, or slightly below 0° C., and the reaction was allowed to proceed very slowly. A tough viscous paste sometimes formed during the course of the nitration, but ordinarily in the presence of a sufficient quantity of acid, the mixture could be kept in motion without difficulty. After all the nitrile had been added, the yellow syrup was kept in a refrigerator for several hours. During this time it darkened perceptibly and formed a deeply colored yellowish-brown solution. This was cautiously poured on ice, and the resulting light-yellow, flocculent product filtered by suction. After washing with water, dilute ammonium hydroxide, and again with water, the substance was sufficiently pure for further work.

To obtain a perfectly pure compound, the crude product was added, without previous drying, to warm acetic anhydride and the solution kept at its boiling point for a few minutes. It was then diluted with water to destroy the excess of anhydride, heated, and allowed to cool. The nitrile separated in yellow prisms. On recrystallization from alcohol, long, lustrous, pale-yellow needles were obtained which melted constantly at 131.5° C. (cor.). The product is soluble in hot water, alcohol, and benzol, and partially soluble in ether. It is insoluble in cold carbon tetrachloride; partially soluble in this solvent at its boiling point. The best yield of crude nitro-nitrile recorded was about 9 grams (approximating 74 per cent. of the theoretical). The average nitration, however, yielded about 65 per cent. of the theory. On analysis:

0.1088 gram of substance gave 19.4 cc. of moist nitrogen at 17.5° C. and 763.5 mm.

| | Found. | Calculated for $C_9H_7O_3N_3$. |
|---|---|---|
| N | 20.74 | 20.49 |

The temperature conditions in the production of this nitro compound must be rather carefully followed in order to get uniform results. A marked rise in temperature is to be avoided, since in several experiments this gave mixtures of other nitration products that have not been studied or identified.

### 2. *Saponification of the Nitrile.*

In order to definitely locate the position of the nitro group, the nitro-acetaminobenzonitrile was saponified by boiling under a return condenser for several hours with a solution of alcoholic potassium hydroxide. On heating, the mixture deepened to a beautiful reddish-purple, and ammonia was given off. When cool, the solution deposited the potassium salt, as a crop of orange needles. The salt was dissolved in water, and decomposed with warm, dilute sulphuric acid. The acid recrystallized from dilute alcohol, separated in rich brownish-yellow needles, possessing a splendid golden luster. These, after drying at 110° C., and finally *in vacuo*, were heated in a sealed melting point tube. They began to sublime at 190–200° C., forming a yellow coating on the sides of the tube. At 277–8° C. (uncor.) this coating began to clear and above this point there was decided softening. At 290–291° C. (uncor.) the substance decomposed. This decomposition point was not changed by further recrystallization. Salkowski[36] and Ritsert and Epstein[37] report the melting point of 3-nitro-4-aminobenzoic acid as 284° C. On analysis:

I. 0.1136 gram of substance gave 15.2 cc. of moist nitrogen at 23° C. and 758.5 mm.

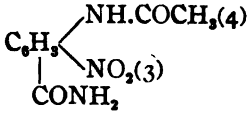
II. 0.0860 gram of substance gave 11.35 cc. of moist nitrogen at 19.5° C. and 766.5 mm.

| | Found. | Calculated for $C_7H_6O_4N_2$. |
|---|---|---|
| N | I. 15.05 | 15.39 |
| | II. 15.27 | ... |

Bogert and Kropff[38] have described the only other possible nitraminobenzoic acid that can theoretically be formed (*i. e.*, the 2-nitro-4-aminobenzoic acid). This substance takes the form of bronze scales which melt at 239.5° C. (cor.).

As a further check on the correctness of this work, 3-nitro-4-aminobenzoic acid was synthesized directly from pure para-aminobenzoic acid by the method outlined by Ritsert and Epstein,[37] which is in part the nitration described by Kaiser.[35] This nitro-acid, when crystallized to constant fusion point from alcohol decomposed at about 290.5° C. (uncor.), showing tendencies toward sublimation and previous softening similar to those manifested by the compound derived from the nitrile. A mixture of the two acids decomposed at 290° C. (uncor.).

### 3. *3-Nitro-4-acetaminobenzamide.*



$$\underset{\displaystyle CONH_2}{C_6H_3}\left<\begin{matrix}NH.COCH_3(4)\\NO_2(3)\end{matrix}\right.$$

3-Nitro-4-aminobenzamide has been adequately described by Grohmann,[39] and Thieme.[40] The former prepared it by heating 4-brom-3-nitrobenzamide with alcoholic ammonia at 180° C., and the latter by treating ethyl 3-nitro-4-aminobenzoate with ammonium hydroxide. The acetyl derivative of this compound, in spite of numerous attempts on the part of Thieme,[40] has apparently not been reported in the chemical literature.

It was prepared in the course of this work, by the following method:

3-Nitro-4-acetaminobenzonitrile was added to a 3 per cent. solution of hydrogen peroxide (rendered slightly alkaline to phenolphthalein). Heated on a water bath for one to two hours, the substance appeared to change in consistency but only part of it entered solution. A small amount of acetic anhydride was then added, and the mixture gradually taken to dryness. The residue was taken up with water and filtered. The residual, yellow, granular mass was found soluble in warm alcohol. It crystallized from this solution in lustrous, yellow plates. On further recrystallization from the same solvent, the substance crystallized in yellow, flat, branching needles, and melted constantly at 239.5° C. (uncor.) with previous softening and sublimation at about 215° C.

The amide is soluble in hot alcohol, less soluble in the cold solvent, very slightly soluble in boiling chloroform, appreciably soluble in hot water. It is apparently insoluble in cold water, chloroform, and in ether and benzol at their boiling points. On analysis:

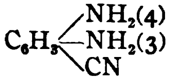
0.1143 gram of substance gave 18.85 cc. of moist nitrogen at 19.5° C. and 757 mm.

| | Found. | Calculated for $C_9H_9O_4N_3$. |
|---|---|---|
| N | 18.84 | 18.84 |

On heating the compound with KOH, ammonia was evolved, the solution turned purple, and on adding a little alcohol and cooling, precipitated the typical potassium salt of 3-nitro-4-aminobenzoic acid.

## REDUCTION OF 3-NITRO-4-ACETAMINOBENZONITRILE.

### 1. *3,4-Diaminobenzonitrile.*



$$C_6H_3\begin{cases}NH_2(4)\\NH_2(3)\\CN\end{cases}$$

The acid, corresponding to this nitrile was prepared by Griess[41] [42] from 4-nitro-3-aminobenzoic acid, and by Salkowski[36] and Griess[43] from 3-amino-4-nitrobenzoic acid. Its structure was readily shown by the elimination of carbon dioxide and the production of ortho-phenylene diamine.

The nitrile was obtained by reducing 5 grams of 3-nitro-4-acetaminobenzonitrile with 25 grams of stannous chloride in 100 cc. of concentrated hydrochloric acid. The temperature of the mixture was maintained at about 40° C. and the addition of the nitro-product was very gradual. Complete solution resulted, the deep-yellow color growing paler but never entirely disappearing. In this case no double tin salt separated. After standing over night in the ice box, the solution was placed in a freezing mixture, diluted with cold water, covered with a layer of ether and very slowly neutralized with a concentrated solution of potassium hydroxide. The temperature was not permitted to rise above 20° C.

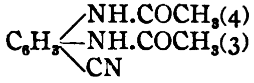
The free base was extracted four times with ether, the ethereal solutions dried over calcium chloride, and cautiously evaporated. Ether proved a very poor solvent for this nitrile, but chloroform extractions gave no better results, and an effort to "de-tin" the solution with hydrogen sulphide, neutralizing carefully and evaporating to low bulk, failed to give the desired product. The best yield of diamine recorded was about 33–34 per cent. of the theoretical.

The residue from ether was colorless or faintly colored after drying in vacuo, but soon turned pink in the air. Crystallized to constant melting point from water, it fused at 147.5° C. (cor.). The substance is soluble in boiling water, alcohol, and hot chloroform, but difficultly soluble in cold chloroform and ether. On analysis:

0.1508 gram of substance gave 42.3 cc. of moist nitrogen at 21.5° C. and 755 mm.

| | Found. | Calculated for $C_7H_7N_3$. |
|---|---|---|
| N | 31.64 | 31.58 |

2. *3,4-Diacetdiaminobenzonitrile.*



$$C_6H_3\begin{cases} NH.COCH_3(4) \\ NH.COCH_3(3) \\ CN \end{cases}$$

The diamine was treated with acetic anhydride and dissolved readily without immediate evolution of heat. After warming on the hot plate for a few minutes a white crystalline mass was thrown out of solution. Water was subsequently added, and the solution heated to destroy the excess of anhydride and to dissolve the crude acetyl derivative. The product crystallized on cooling. It forms silky needles, which (especially after recrystallization from water) form a bulky, absorbent mass, matting down closely on the filter paper. The amounts obtained are usually very satisfactory but in several acetylations, impurities (perhaps higher acetyl derivatives) were obtained which could not readily be separated from the diacetyldiamine and which sensibly diminished the yield.

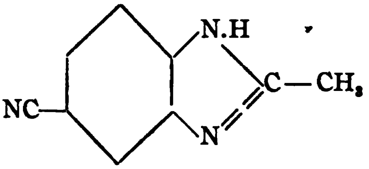
The pure compound melted at 238–238.5° C. (uncor.), decomposing just above its point of liquefaction. It was found soluble in cold glacial acetic acid, cold alcohol and boiling water, difficultly soluble in hot chloroform and benzol, and insoluble in ether at its boiling point. On analysis:

0.123 gram of substance gave 21 cc. of moist nitrogen at 21° C. and 750 mm.

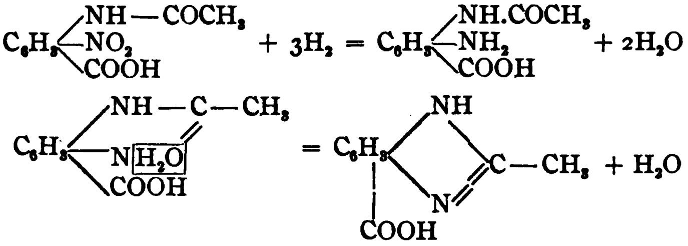
| | Found. | Calculated for $C_{11}H_{11}O_2N_3$. |
|---|---|---|
| N | 19.17 | 19.36 |

The acid of which the above diacetyl derivative is the nitrile, was prepared by Zehra[44] by an entirely analogous method.

### 3. *3-Cyan-α-methyl Benzimidazole.*

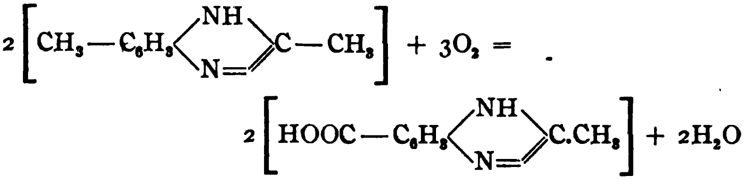


Kaiser[35] prepared what he termed "anhydrodiacetdiaminobenzoic acid" by reducing the 3-nitro-4-acetamino, and 4-nitro-3-acetamino benzoic acids. The following reactions show the course of the reduction and subsequent condensation:



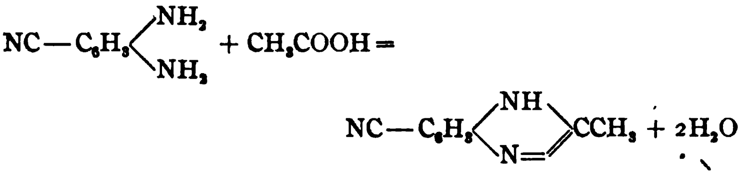
$$C_6H_3\begin{cases}NH-COCH_3\\NO_2\\COOH\end{cases} + 3H_2 = C_6H_3\begin{cases}NH.COCH_3\\NH_2\\COOH\end{cases} + 2H_2O$$

Some years later, the same product was obtained by Bamberger and Berle,[45] by the action of potassium permanganate on the dimethyl benzimidazole, which was oxidized to the meta carboxylic acid.


2 CH₃—C₆H₃ NH N= C—CH₃ + 3O₂ =
2 HOOC—C₆H₃ NH N= C.CH₃ + 2H₂O

The nitrile of this acid was prepared by two methods.

(*a*) The diaminobenzonitrile was boiled with a large excess of glacial acetic acid for an hour and three-quarters, and the mixture distilled to small volume. The remaining acid was neutralized with sodium carbonate, and the precipitated product extracted repeatedly with ether. After evaporating the ethereal solution and recrystallizing from water, the substance melted at about 241° C. (uncor.). The compound formed according to the following equation:



$$NC-C_6H_3\left\langle\begin{matrix}NH_2\\NH_2\end{matrix}\right. + CH_3COOH = NC-C_6H_3\left\langle\begin{matrix}NH\\N=\end{matrix}\right\rangle CCH_3 + 2H_2O$$

(*b*) Owing to the insignificant yield obtained by the first method, the substance was made by heating the diacetdiaminobenzonitrile just above its melting point. (If taken to 250–260° C. decided charring results). The melt boiled and gave off vapors of acetic acid. On cooling, the mass usually solidified to a gray cake or formed a viscous resin. It was most conveniently extracted with boiling water and boneblacked (if the previous decomposition gave a resinous body). Faintly colored granules were deposited from the aqueous solution on cooling, and were repeatedly crystallized from the same solvent.

The benzimidazole is usually obtained in the form of dull, granular, coral-like clusters of microscopic crystals, sometimes in opaque rods. It melts at 241° C. (uncor.), is readily soluble in cold acetone, glacial acetic acid, boiling water and amyl acetate, soluble in cold alcohol, very difficultly soluble in boiling ether and chloroform, and apparently insoluble in hot carbon tetrachloride. The substance sublimes, forming a shimmering, tinsel-like, crystalline sublimate. On analysis:

I. 0.1501 gram of product gave 0.3753 gram of carbon dioxide and 0.062 gram of water.

II. 0.108 gram of substance gave 25 cc. of moist nitrogen at 19° C. and 758 mm.

III. 0.09885 gram of substance gave 23 cc. of moist nitrogen at 21.5° C. and 757.5 mm.

|   | Found. I. | Found. II. | Found. III. | Calculated for $C_9H_7N_3$. |
|---|---|---|---|---|
| C | 68.19 | ... | ... | 68.75 |
| H | 4.63 | ... | ... | 4.49 |
| N | ... | 26.55 | 26.33 | 26.76 |

As in the case of the diacetyl derivative, the benzimidazole was also at times contaminated with other compounds, which have not been identified, and which could only be eliminated by repeated crystallization.

### 4. *Action of Tin and Acetic Acid on 3-Nitro-4-acetaminobenzonitrile.*

In an effort to gain the cyan-methyl-benzimidazole by the method of Hübner,[46] 5 grams of nitro-acetaminobenzonitrile were added to glacial acetic acid, together with 10 grams of metallic tin. Apparently little reduction took place, and in order to insure ionization of the acetic acid, water was added to the mixture. The reaction was by no means vigorous, and the reduction was allowed to proceed at the boiling point, under a reflux condenser, for nine and one-quarter hours. On cooling, the deep red solution was filtered from a residue of tin and tin salts. On examination, it was found to contain none of the starting product. The solution was rendered slightly alkaline with a cold solution of caustic potash, and allowed to stand over night. A small precipitate from which nothing was isolated was filtered off. The clear filtrate, however, on careful addition of cold acetic anhydride, yielded a crystalline, faintly colored product, which was soluble in an excess of the precipitating agent. No evolution of heat was noticed. The crude product was also soluble in hot alcohol, water, in ether, and in benzol. It was thoroughly boneblacked, crystallized twice from water, and subsequently twice from alcohol. From the last named solvent, it crystallized in small, slender, colorless needles. Its melting point was not very sharp, decomposition setting in at about 270° C. (uncor.). The purified product has solubilities that differ in some respects from those of the crude substance. It was found soluble in hot water, alcohol, and glacial acetic acid, practically insoluble in boiling ether, chloroform, and benzol. On analysis:

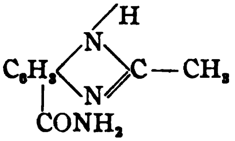
I. 0.1421 gram of substance gave 0.3215 gram of carbon dioxide and 0.0574 gram of water.

II. 0.1192 gram of substance gave 25.65 cc. of moist nitrogen at 21.5° C. and 760 mm.

III. 0.11855 gram of substance gave 26.1 cc. of moist nitrogen at 21.5° C. and 747 mm.

| | Found. | | | Calculated for |
|---|---|---|---|---|
| | I. | II. | III. | $C_9H_9ON_3$. |
| C | 61.70 | ... | ... | 61.68 |
| H | 4.53 | ... | ... | 5.18 |
| N | ... | 24.44 | 24.57 | 24.00 |

The product may therefore be the methyl benzimidazole, 3 carbamide



although too small an amount for further investigation was obtained.

# SUMMARY.

1. Para-aminobenzonitrile may be readily obtained through the reduction of para-nitrobenzonitrile with stannous chloride and hydrochloric acid.

2. The amino group of the nitrile undergoes the usual reactions with acid chlorides, anhydrides, and esters, to form the corresponding cyananilides.

3. The amino group, furthermore, forms substituted ureas with phosgene and the cyanates.

4. The nitrile group may in general be saponified to the amide by means of alkaline hydrogen peroxide.

5. The benzene ring, when the amino group is protected by acetylation, may be brominated and nitrated, mono derivatives being obtained in either case. The nitro group occupies a position which is ortho to the acetamino radical.

6. 3-Nitro-4-acetaminobenzonitrile may be reduced to the cyan-ortho-phenylenediamine, which may be converted to the corresponding cyan-methyl-benzimidazole as well as the intermediate diacetyl compound.

# BIBLIOGRAPHY.

1. Beilstein and Reichenbach, *Annalen*, 132, 144 (1864).
2. Engler, *Zeitschrift fur Chemie*, 11, 613 (1868).
3. Engler, *Annalen*, 149, 297 (1869).
4. Fricke, *Berichte*, 7, 1321 (1874).
5. Fricke, "*Ueber Nitro und Amido benzonitrile*," *Inaugural Dissertation*, Göttingen (1874).
6. Griess, *Berichte*, 8, 861 (1875).
7. Reid, *Am. C. J.*, 21, 290 (1899).
8. Bogert and Kohnstamm, *Jour. Am. Chem. Soc.*, 25, 478 (1903).
9. Bogert and Hand, *Jour. Am. Chem. Soc.*, 24, 1035 (1902).
10. Sandmeyer, *Berichte*, 18, 1492 (1885).
11. Hantzsch and Schulze, *Berichte*, 28, 675 (1895).
12. Claus, *Jour. prak. Chem.*, [2] 51, 404 (1895).
13. Langen, *Inaugural Dissertation*, Freiburg (1888).
14. Borsche, *Berichte*, 42, 3597 (1909).
15. *U. S. Patents*, 531973–531977 (included).
16. Schraube and Schmidt, *Berichte*, 27, 514 (1894).
17. Bogert and Beans, *Jour. Am. Chem. Soc.*, 26, 466 (1904).
18. Schraube and Schmidt, *Berichte*, 27, 520 (1894).
19. Niementowski, *Berichte*, 34, 3325 (1901).
20. Radziszewski, *Berichte*, 18, 355 (1885).
21. Reitsert and Grube, *Berichte*, 42, 3713 (1909).
22. Bogert and Beans, *Jour. Am. Chem. Soc.*, 26, 484 (1904).
23. Bogert and Williamson, *Unpublished work*.
24. Michael, *Berichte*, 10, 576 (1877).
25. Pinner, *Berichte*, 16, 1654, *et al.* (1883).
26. Griess, *Jour. prak. Chem.*, [2] 5, 369 (1872).
27. Guareschi, cf. *Beilstein*, [3] *Vol.* 2, 1272.
28. Grube, "*o-Amidobenzonitrile*," *Inaugural Dissertation*, Marburg (1909).
29. Senier and Goodwin, *Lond. Chem. Jour.*, 81, 283 (1902).
30. Eibner, *Annalen*, 302, 361 (1898).
31. Diels and Seib, *Berichte*, 42, 4065 (1909).
32. Wheeler and Weller, *Jour. Am. Chem. Soc.*, 24, 1063 (1902).
33. Bogert and Beans, *Jour. Am. Chem. Soc.*, 26, 494 (1904).
34. Rhode, *Berichte*, 25, 2053 (1892).
35. Kaiser, *Berichte*, 18, 2943 (1885).
36. Salkowski, *Annalen*, 173, 54 (1874).
37. Ritsert and Epstein, *D. R. P.*, 151725; *Friedlander, Part* 7, 644 (1903–'04).
38. Bogert and Kropff, *Jour. Am. Chem. Soc.*, 31, 847 (1909).
39. Grohmann, *Berichte*, 23, 3449 (1890).
40. Thieme, *Jour. prak. Chem.*, [2] 43, 457 (1891).
41. Griess, *Berichte*, 2, 435 (1869).
42. Griess, *Berichte*, 5, 199 (1872).
43. Griess, *Berichte*, 5, 856 (1872).
44. Zehra, *Berichte*, 23, 3632 (1890).
45. Bamberger and Berle, *Annalen*, 273, 324 (1893).
46. Hübner, *Annalen*, 209, 353 (1881).